The "effective amount" has been amended to read "amount effective for the treatment of the symptoms of Parkinson's syndrome." Thus, what the amount is effective for is now recited, thus overcoming the 35 U.S.C. 112, first paragraph, rejection directed to the recitation of "effective."

The 35 U.S.C. 102(b) rejections of claims 18-20, 22 and 31 as being anticipated by Chiang et al. and of claim 18 as being anticipated by WO '468 and the 35 U.S.C. 103(a) rejection of claims 18-33 as being unpatentable over Chiang et al and/or WP '468 individually or in combination are respectfully traversed for the following reasons.

The transdermal therapeutic system of the present invention is an improved simple matrix system. In such systems, the drug is dissolved or dispersed in the pressure-sensitive adhesive. In case of the inventive transdermal therapeutic systems, (-)-5,6,7,8-tetrahydro-6-[propyl-1[2-(2-thienyl) ethyl]amino]-1-naphthalenol is dissolved in a pressure-sensitive adhesive based on silicone adhesives or acrylate adhesives. The drug is present as free base within the simple matrix of the transdermal therapeutic system.

In contrast, both Chiang et al. and WO 94/07468 teach the use of a salt of the drug, namely its hydrochloride. The use of the (-)-5,6,7,8-tetrahydro-6-[propyl-1[2-(2-thienyl) ethyl]amino]-1-naphthalenol hydrochloride causes the formation of a two-phase matrix system for transdermal administration of this drug, because the salt of the drug is substantially insoluble in the hydrophobic polymer component of the matrix. The adhesive matrix of a two phase matrix system includes particulate hydrated hydrophilic material that contains the drug and that particulate material constitutes a phase with substantial particulate contact.

The two phases of Chiang et al. are the surfactant (Tween 20)-containing silicone adhesive solution and the drug-containing MicroCel E, which is a calcium silicate powder. Both phases are combined and then cast. Figure 1 and tables 1 and 2 of Chiang et al illustrate the skin flux and the release of (-)-5,6,7,8-tetrahydro-6-[propyl-1[2-(2-thienyl) ethyl]amino]-1-naphthalenol from simple matrix systems and the two phase matrix system. The results provided by Chiang et al. would not suggest that there is a reasonable expectation of success to realize a simple matrix system for transdermal therapeutic administration of (-)-5,6,7,8-tetrahydro-6-[propyl-1[2-(2-thienyl) ethyl]amino]-1-naphthalenol, because a 10 times increase in drug release was observed in a

two-phase matrix in comparison to a simple polymer matrix (page 711, left column, 2nd paragraph).

WO '468 teaches two-phase matrices for sustained drug delivery devices in which the adhesive matrix includes particulate hydrophilic material that contains the drug and possesses substantial particle-to-particle contact (page 6, last paragraph). WO '468 teaches hydrated inorganic silicate particles to be the hydrophilic material and specifies that the unhydrated silicate normally constitutes about 2 to 20% by weight of the matrix, more usually 4 to 10% by weight. The experimental results provided in this reference (page 11, table 1) indicate that hardly any skin flux can be achieved with simple matrix systems and that only two-phase systems allow a reasonable skin flux.

Thus, neither Chiang et al. nor WO '468 discloses the subject matter of amended claim 18. In addition, neither reference provides any motivation to those with ordinary skill in the art to refrain from the two-phase systems and to expect that a simple matrix system would be capable of allowing administration of (-)-5,6,7,8-tetrahydro-6-[propyl-1[2-(2-thienyl) ethyl]amino]-1-naphthalenol with reasonable flux rates.

It is, therefore, believed the application is in condition for allowance.

Applicants also note that the corresponding European patent application was allowed for grant (EP 1 033 978).

A one month extension of time is hereby requested for which please charge the $110.00 official fee to Deposit Account No. 10-1250. Also, charge any fee deficiency or credit any excess payment to the same deposit account.

Respectfully submitted,

Jordan and Hamburg LLP

By _____
C. Bruce Hamburg
Reg. No. 22,389
Attorney for Applicants

Jordan and Hamburg LLP
122 East 42nd Street
New York, New York 10168
(212) 986-2340

CBH/pb

APPENDIX I

AMENDED CLAIMS WITH AMENDMENTS INDICATED THEREIN BY BRACKETS AND UNDERLINING

18. (Amended) A transdermal therapeutic system comprising a self-adhesive matrix layer containing the free base (-)-5,6,7,8-tetrahydro-6-[propyl-1[2-(2-thienyl) ethyl]amino]-1-naphthalenol in an [effective] amount effective for the treatment of the symptoms of Parkinson's syndrome, wherein the matrix is based on a non-aqueous, acrylate-based or silicone-based polymer adhesive system having a solubility of ≥5% (w/w) for the free base (-)-5,6,7,8-tetrahydro-6-[propyl-[2-(2-thienyl) ethyl]-amino]-1-napthalenol [, and wherein said matrix is substantially free of inorganic silicate particulates]; a backing layer inert to the components of the matrix layer; and a protective foil or sheet covering the matrix layer to be removed prior to use.